

## CLAIMS

1. – 52. (CANCELLED)

53. (CURRENTLY AMENDED) A method of estimating arterial delay and arterial dispersion ( $t$ ,  $\alpha$ ,  $\sigma$ ) values for outputting blood perfusion indices for a region of interest (ROI) by from operating a computer program on intensity data in input to a computer comprising:

- a. using a computer to apply applying a first gamma-variate function (GVF) to an arterial input function (AIF<sub>a</sub>) using a computer to provide an estimated first model of a vascular transport function  $h_a(t)$ , wherein for  $t <$

10  $t_1$ ,  $h_a(t) = 0$  and for  $t \geq t_1$ ,  $h_a(t) = \frac{1}{\sigma_1} (t - t_1)^{\alpha_1} e^{-(t-t_1)/\sigma_1}$ , wherein ~~an~~

estimated  $t_1$  is the transit time of a contrast agent from a measured initial said AIF<sub>a</sub> to a region of interest (ROI) and  $\sigma_1$  is an estimating an initial delay value of said contrast agent, wherein said  $\sigma_1 = (t_1)(\beta_1)/(1-\beta_1)$ , wherein said  $\beta_1$  is a known relative dispersion value having a range from 0 to 1;

15 b. estimating an initial value  $\sigma_+$  of said contrast agent, wherein said  $\sigma_+ = (t_+)(\beta_+)/((1-\beta_+))$ , wherein said  $\beta_+$  is a known relative dispersion value having a range from 0 to 1;

- b. using a computer to convolve convolving AIF<sub>a</sub>( $t$ ) with said  $h_a(t, \alpha_+=0)$  h<sub>a</sub>(t) with  $\alpha_1=0$  using a computer for obtaining an arterial input function  $AIF_t(t) = AIF_a(t) \otimes h_a(t, \alpha_+=0)$  h<sub>a</sub>(t) with  $\alpha_1=0$  at said ROI;

20 c. using a computer to estimate estimating a blood flow rate  $F_t$  and a tissue impulse residue function  $R_e(t)$  using a computer by deconvolving a

concentration curve  $C(t) = (F_t/k_H)AIF_t(t) \otimes R_e(t)$ , wherein  $k_H$  is a ~~hermoerit hermatocrit~~ correction constant having a known value; and

d. using a computer to optimize said mean transit time and dispersion ( $t_2$ ,

$\alpha_2, \sigma_2$ ) values using a least squares method; and

5 e. using a computer to output said outputting estimated and optimized tissue mean transit time and dispersion ( $t_2, \alpha_2, \sigma_2$ ) values from an estimated transport function  $h_e(t)$  for input to a simulated transport function  $h_s(t)$ , wherein a simulated tissue impulse residue function  $R_s(t)$  is determined, wherein a simulated concentration curve  $C_s(t)$  is fitted to said measured  $C(t)$  and quantitative said blood perfusion indices are calculated,  
10 wherein each said step is performed by a suitably programmed computer.

54. (PREVIOUSLY PRESENTED) The method of claim 53, wherein said intensity data is generated by administering a contrast agent to a body lumen  
15 of a body during a dynamic imaging scan, wherein said body lumen comprises an artery or vein, wherein an image response from said contrast agent is recorded to computer data storage in a computer.

55. (PREVIOUSLY PRESENTED) The method of claim 53, wherein said  $C(t)$  is a  
20 temporal concentration of said contrast agent obtained from said intensity data, wherein said intensity data comprises contrast images sequentially acquired from a region in a body, whereby said contrast agent concentration is plotted versus time.

56. (PREVIOUSLY PRESENTED) The method of claim 53, wherein said AIF<sub>a</sub> is based on a measured early arrival contrast agent peak intensity from a feeding blood vessel to said ROI.

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57. (PREVIOUSLY PRESENTED) The method of claim 53, wherein said AIF<sub>a</sub> is scaled upward according to a venous input function (VIF), wherein said VIF is based on a measured late arrival contrast agent peak intensity from a large vein draining from said ROI.

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58. (PREVIOUSLY PRESENTED) The method of claim 53, wherein said estimated transit time  $t_1$  is the transit time of said contrast agent from a measured initial said AIF<sub>a</sub> of said contrast agent C(t) in a body lumen to said ROI, wherein said  $t_1$  is estimated from plots of said AIF<sub>a</sub> versus time and said C(t) versus time.

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59. (CURRENTLY AMENDED) The method of claim 53, wherein said  $h_a(t)$  is calculated using said estimated transit time  $t_1$  and said estimated dispersion value  $\sigma_1$ , wherein  $h_a(t, \alpha_4=0)$   $h_a(t)$  with  $\alpha_1=0$  is plotted versus time.

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60. (PREVIOUSLY PRESENTED) The method of claim 53, wherein said estimated transport function  $h_e(t)$  is calculated using the relation  $h_e(t) = -\frac{dR_e(t)}{dt}$ .

61. (CURRENTLY AMENDED) The method of claim 53, wherein said tissue mean transit time and dispersion ( $t_2$ ,  $\alpha_2$ ,  $\sigma_2$ ) values are estimated from said estimated transport function  $h_e(t)$ , wherein said  $t_2$ , said  $\sigma_2$  and said  $\alpha_2$  are input to a simulated transport function  $h_s(t)$ , wherein said  $h_s(t)$  is ~~said~~ a second gamma-variate function.

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62. (PREVIOUSLY PRESENTED) The method of claim 53, wherein said simulated tissue impulse resistive function  $R_s(t)$  is determined using the

10 relation  $R_s(t) = 1 - \int_0^t h_s(\tau) d\tau$ .

63. (PREVIOUSLY PRESENTED) The method of claim 53, wherein said simulated concentration curve  $C_s(t)$  is determined using the relation  $C_s(t) =$

$$(F_t/k_H)AIF_t(t) \otimes R_e(t) = (F_t/k_H) \int_0^t AIF_t(t) R_e(t-\tau) d\tau.$$

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64. (PREVIOUSLY PRESENTED) The method of claim 53, wherein said  $F_t$ , said  $t_1$ , said  $\sigma_1$ , said  $\alpha_2$ , said  $t_2$ , said  $\alpha_2$ , and said  $\sigma_2$  are optimized by a least squares method to fit said  $C_s(t)$  to said  $C(t)$ .

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65. (PREVIOUSLY PRESENTED) The method of claim 53, wherein said perfusion indices have the relations:

f. blood flow (BF) =  $F_t$ ;

- g. Mean Transit Time (MTT) =  $t_2 + \sigma_2(1+\alpha_2)$ ;
- h. Blood Volume (BV) = BF \* MTT;
- i. Arterial Delay (DT) =  $t_1 + \sigma_1(1+\alpha_1)$ ;
- j. Arterial Dispersion time (ADT) =  $\sigma_1 \sqrt{1+\alpha_1}$ ;
- 5 k. Tissue Dispersion Time (TDT) =  $\sigma_2 \sqrt{1+\alpha_2}$ ;
- l. Relative Arterial Dispersion (RAD) = ADT/DT; and
- m. Relative Tissue Dispersion (RTD) = TDT/MTT.

66. (PREVIOUSLY PRESENTED) The method of claim 53, wherein said AIF<sub>t</sub>(t)  
10 is measureable in a small lumen showing a delay relative to said AIF<sub>a</sub>(t),  
wherein optimized values for said  $\sigma_1$  and said  $t_1$  are determined by fitting said  
simulated AIF<sub>t</sub>(t) to said measured AIF<sub>t</sub>(t), wherein said relative dispersion  $\beta_1$   
is determined and applied to all other said intensity data of said ROI using said  
15  $\beta_1$ , wherein a more robust fitting process is provided by a reduced number of  
parameters for optimization.

67. (PREVIOUSLY PRESENTED) The method of claim 66, wherein when  
said relative dispersion  $\beta_1$  is determined, said vascular transport function  
20  $h_a(t)$  is described by a single variable said  $t_1$  with a constant said  $\beta_1$ ,  
wherein a two-step method is used to determine said delay and said  
dispersion values comprising:  
a. deriving an initial tissue impulse residue function  $R_0(t)$  by  
deconvolving  $C(t) = (F_0/k_H)AIF_a(t) \otimes R_0(t)$  using a model-free singular

value decomposition (SVD) method, wherein said time delay  $t_1$  is determined by a maximum position of said  $R_0(t)$  at  $R_{0\max}(t=t_1)$ ; and

- b. determine said  $AIF_t(t)$  at an input of said ROI using said  $h_a(t)$  with said  $t_1$  and said  $\beta_1$  held constant, wherein said  $\sigma_1$  is determined.

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68. (PREVIOUSLY PRESENTED) The method of claim 67, wherein a value of tissue blood flow  $F_t$  and a corrected impulse residue function  $R_e(t)$  are obtained by deconvolving  $C(t) = (F_t/k_H)AIF_t(t) \otimes R_e(t)$  using said SVD method, wherein said perfusion indices are determined from a curve of said  $R_e(t)$ , wherein  $MTT = \int_0^\infty R_e(\tau)d\tau$ ,  $BF=F_t$ , and  $BV=BF*MTT$ .

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69. (PREVIOUSLY PRESENTED) The method of claim 53, wherein said contrast agent is in a tissue ROI having a tissue mean transit time  $\tau$ , wherein a tissue impulse residue function is approximated by the relation  $R(t > \tau) = Ee^{-k(t-\tau)}$  and  $R(t \leq \tau) = 1$ , wherein  $E$  is an extraction fraction of said contrast agent in said tissue, wherein  $k$  is a constant clearance rate of said contrast agent diffusing from said tissue having a relation  $k = E*F_t/V_e$ , wherein  $V_e$  is the volume fraction of extravascular and extracellular space (EES) in said tissue.

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70. (PREVIOUSLY PRESENTED) The method of claim 69, wherein said tissue impulse residue function  $R_s(t)$  of said simulated concentration curve  $C_s(t)$  is replaced by an average impulse residue function that incorporates

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said contrast agent leaked out of a blood vessel into said tissue and gradually clearing from said tissue, wherein said simulated concentration curve  $C_s(t)$  is fitted to said measured  $C(t)$  and quantitative said blood perfusion indices are calculated, wherein said  $E$  and said  $V_e$  are additional parameters optimized with other adjustable parameters using a least squares method.